



Image

1617

PATENT
ATTORNEY DOCKET NO. 00742/057002

Certificate of Mailing: Date of Deposit: February 26, 2004

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Rosemarie Perullo

Printed name of person mailing correspondence

Rosemarie Perullo
Signature of person mailing correspondence

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Junying Yuan <i>et al.</i>	Art Unit:	1617
Serial No.:	09/829,040	Examiner:	Wang, Shengjun
Filed:	April 9, 2001	Customer No.:	21559
Title:	METHODS AND COMPOUNDS FOR DECREASING CELL TOXICITY OR DEATH		

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Applicants submit the references listed on the enclosed Form PTO-1449, copies of which are enclosed. A copy of a communication from a foreign patent office in a counterpart application is also enclosed.

Submission of this statement is not a representation that a search has been made, nor is the inclusion of information in this statement an admission that the information is material to patentability.

This statement is being filed after the mailing of a first Office action on the merits,

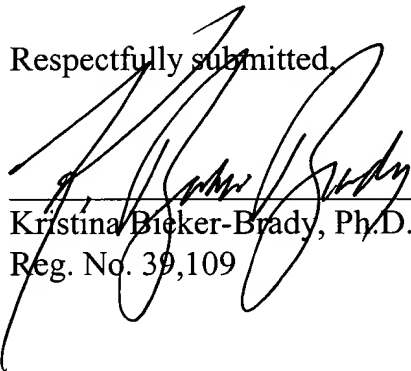
but before the mailing of a final Office action or a Notice of Allowance. I, the undersigned, hereby certify that each item of information contained in this statement was first cited in any communication from a foreign patent office in a counterpart foreign application, dated December 11, 2003, which is not more than three months prior to the filing of this statement

If there are any other charges or any credits, please apply them to Deposit Account No. 03-2095.

Date:

February 16, 2004

Respectfully submitted,



Kristina Bieker-Brady, Ph.D., P.C.
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PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:
KRISTINA BIEKER- BRADY
CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

ACTION DUE Replied
DUE DATE 1-11-04
INITIALS mh/w

PCT

DEC 15 2003

WRITTEN OPINION

(PCT Rule 66)

Applicant's or agent's file reference 00742/057WO2		Date of Mailing (day/month/year) 11 DEC 2003 REPLY DUE within 1 months/days from the above date of mailing
International application No. PCT/US02/11025	International filing date (day/month/year) 09 April 2002 (09.04.2002)	Priority date (day/month/year) 09 April 2001 (09.04.2001)
International Patent Classification (IPC) or both national classification and IPC IPC(7): A61K 31/13, 31/16, 31/42, 31/70, 31/56, 31/50, 31/135, 31/165, 31/425, 31/445, 31/505, 33/08 and US Cl.: 514/34, 178, 245, 249, 275, 331, 367, 380, 599, 617, 622, 624, 625, 638, 646; 424/692		
Applicant PRESIDENT AND FELLOWS OF HARVARD COLLEGE		

1. This written opinion is the first (first, etc.) drawn by this International Preliminary Examining Authority.
2. This opinion contains indications relating to the following items:
 - I ☒ Basis of the opinion
 - II ☐ Priority
 - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - IV ☐ Lack of unity of invention
 - V ☒ Reasoned statement under Rule 66.2 (a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - VI ☐ Certain documents cited
 - VII ☐ Certain defects in the international application
 - VIII ☐ Certain observations on the international application
3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. ~~The applicant may, before the expiration of that time limit, request this Authority to grant an extension. See rule 66.2(d).~~

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.
For an informal communication with the examiner, see Rule 66.6

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.
4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 09 August 2003 (09.08.2003)

Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703)305-3230	Authorized officer Shengjun Wang <i>Janice Ford</i> Telephone No. (703) 305-1235
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Form PCT/IPEA/408 (cover sheet)(July 1998)

WRITTEN OPINION

International application No.

PCT/US02/11025

I. Basis of the opinion

1. With regard to the elements of the international application:*

- ☒ the international application as originally filed
- ☒ the description:
 pages 1-54 _____, as originally filed
 pages NONE _____, filed with the demand
 pages NONE _____, filed with the letter of _____
- ☒ the claims:
 pages 55-68 _____, as originally filed
 pages NONE _____, as amended (together with any statement) under Article 19
 pages NONE _____, filed with the demand
 pages NONE _____, filed with the letter of _____
- ☒ the drawings:
 pages 1-68 _____, as originally filed
 pages NONE _____, filed with the demand
 pages NONE _____, filed with the letter of _____
- ☐ the sequence listing part of the description:
 pages NONE _____, as originally filed
 pages NONE _____, filed with the demand
 pages NONE _____, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item. These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the written opinion was drawn on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages NONE _____
- ☐ the claims, Nos. NONE _____
- ☐ the drawings, sheets/fig NONE _____

5. ☐ This opinion has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed."

WRITTEN OPINION

International application No.
PCT/US02/11025

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims 1-21	YES
	Claims NONE	NO
Inventive Step (IS)	Claims NONE	YES
	Claims 1-21	NO
Industrial Applicability (IA)	Claims 1-21	YES
	Claims NONE	NO

2. CITATIONS AND EXPLANATIONS

Claims 1-21 meet the criteria set out in PCT Article 33(2), because the prior art does not teach expressly the method herein claimed. Claims 1-21 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

Claim 1-21 lack an inventive step under PCT Article 33(3) as being obvious over Klunk (WO 99/24394) and Cai et al. (WO 96/02250) in view of Klunk et al. and Huang et al.

Klunk et al (WO 99/24394) teaches a method of treating various diseases associated with amyloid deposits comprising administering to a subject in need thereof an amyloid binding agents. The diseases including Huntington diseases. The amyloid binding agents includes analogues of Congo red. See, particularly, the claims, especially, claim 18. Cai et al. teaches method of treating Huntington disease by using haloperidol. See the abstract.

Klunk et al. or Cai et al. does not teach expressly to employ Congo red as the amyloid binding agents. However, Klunk et al. teaches that Congo red and the Congo red analogues employed in '178 are known to be similarly useful as amyloid binding agents for reducing toxicity. See, the abstract. Huang et al. teaches that Congo red binding to the amyloid from Huntington diseases which have expanded polyglutamine segment. See the abstract.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to employ Congo red for treating a subject with Huntington disease.

A person of ordinary skill in the art would have been motivated to employ Congo red for treating a subject with Huntington disease because Congo red is known to be useful as amyloid binding agent, and particularly for binding to amyloid in Huntington disease. As to claim 3, note since Congo red is known to effectively binding to amyloid from Huntington disease, one of ordinary skill in the art would have been motivated to employ Congo red for treating Huntington disease or diseases with similar amyloids to the amyloid found in Huntington disease. Note employment of Congo red or haloperidol for treating Huntington disease would inherently decrease the cell death or toxicity, or decrease aggregation of expanded polyglutamine repeat.

----- NEW CITATIONS -----

WO 99/24394 (KLUNK et al) 20 MAY 1999, see the claims.

WO 96/02250 (CAI et al) 1 FEBRUARY 1996, see the abstract.

KLUNK et al. Chrysamine-G, a lipophilic analogue of Congo red, inhibits Abeta-induced toxicity in PC 12 cells, Life Sciences, 1998, vol. 63, No. 20, pages 1807-1814, see, particularly, the abstract.

Database Medline (Charlestown Massachusetts, USA) Accession No. 1999338865, Amyloid formation by mutant huntingtin: threshold, progressivity and recruitment of normal polyglutamine protein. Somatic Cell and Molecular Genetics, HUANG et al, 1998, vol. 24, No. 4, pages 217-233, Medline Abstract.

WRITTEN OPINION

International application No.
PCT/US02/11025

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

TIME LIMIT:

The time limit set for response to a Written Opinion may not be extended. 37 CFR 1.484(d). Any response received after the expiration of the time limit set in the Written Opinion will not be considered in preparing the International Preliminary Examination Report.



Sheet 1 of 1

SUBSTITUTE FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE (MODIFIED) PATENT AND TRADEMARK OFFICE <p style="text-align: center;">INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary)</p> (37 C.F.R. § 1.98(b))		<table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 30%;">Attorney Docket No.</td> <td>00742/057002</td> </tr> <tr> <td>Serial No.</td> <td>09/829,040</td> </tr> <tr> <td>Applicant</td> <td>Junying Yuan <i>et al.</i></td> </tr> <tr> <td>Filing Date</td> <td>April 9, 2001</td> </tr> <tr> <td>Group</td> <td>1617</td> </tr> <tr> <td>IDS Filed</td> <td>February 26, 2004</td> </tr> <tr> <td>Customer No.</td> <td>21559</td> </tr> </table>	Attorney Docket No.	00742/057002	Serial No.	09/829,040	Applicant	Junying Yuan <i>et al.</i>	Filing Date	April 9, 2001	Group	1617	IDS Filed	February 26, 2004	Customer No.	21559
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U.S. PATENTS OR PATENT APPLICATION PUBLICATIONS																
Examiner's Initials	Patent Number	Issue/Publication Date	Patentee/Applicant	Class	Subclass	Filing Date (If Appropriate)										
FOREIGN PATENT OR PUBLISHED FOREIGN PATENT APPLICATION																
Examiner's Initials	Document Number	Publication Date	Country or Patent Office	Class	Subclass	Translation (Yes/No)										
	WO 96/02250	February 1, 1996	PCT													
	WO 99/24394	May 20, 1999	PCT													
OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PLACE OF PUBLICATION)																
	C.C. Huang et al., "Amyloid Formation by Mutant Huntingtin: Threshold, Progressivity and Recruitment of Normal Polyglutamine Proteins," <i>Somatic Cell and Molecular Genetics</i> , 24(4) pp. 217-33 (1998) (abstract only).															
	W.E. Klunk et al., "Chrysamine-G, A Lipophilic Analogue of Congo Red, Inhibits A β -Induced Toxicity in PC12 Cells," <i>Life Sciences</i> , V. 63, No. 20, pp.1807-1814 (1998).															
EXAMINER			DATE CONSIDERED													
EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with the next communication to applicant.																